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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,205	10/29/2001	Richard Anthony Godwin Smith	62130-0002	2596

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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/936,205	SMITH ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,14,16-22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9, 14, 16-22, 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/31/2007 has been entered.

Status of Claims

Claims 1-8, 10-13, 15, and 23 are cancelled. Claims 9, 14, 16-22, and 24 are pending.

Priority

This application is a 371 of PCT/GB00/00834 filed on 03/08/2000, which claims foreign priority to UNITED KINGDOM 990553.0 filed on 03/10/1999.

Drawings

The Drawings submitted on 09/10/2001 are accepted and approved.

Objections to Specification

The specification is objected to because on pages 12 and 13 of the specification, some paragraphs are crossed out. Thus proper correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 9, 14, 16-22, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim, 9 it is unclear whether there is an order prescribed in subsection (2) of the claim, meaning, can a peptide element be bound to non-peptide element via fragment peptide-fragment or non-peptide? Also, dependent claims 14, 16-22 and 24 are included in this rejection because they depend from rejected claim 9 and do not cure the deficiencies of the independent claim.

In claim 24, the parentheses are unclear, since it is indefinite whether the kidney perfusion solution be SOLTRAN, or is SOLTRAN merely an example of the solution too be used.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 14, 16-22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical

species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

In claim 9, Applicants claim a fragment comprising any sequence of SEQ ID NO:1 having complement inhibitor activity. Therefore, the fragment is reading on

virtually no structure, and only is reading on the activity of the fragment. Therefore, the written description requirement is not satisfied because the structure of the fragment does not correspond with its function. Also, claim 16 doesn't correct this problem because "any sequence according to 2-197 SEQ ID NO:1 reads on fragments of SEQ ID NO:1, for example.

Also, in claim 9, subsection (2)(a), Applicants claim a non-peptidic membrane-binding element that has acyl groups. Therefore, virtually no structure is provided (only acyl group requirement) and only extremely broad function (binding any membrane) is disclosed. Therefore, the written description requirement is not satisfied because the structure of the membrane-binding element does not correspond with its function.

Further, in claim 9, subsection (2)(b), Applicants claim a peptide membrane-binding element that has basic amino acids. Therefore, virtually no structure is disclosed (only at least 2 basic amino acids) and only extremely broad function (binding any membrane) is claimed.

In claim 22, different fragments of peptidic membrane binding elements are claimed that comprise 8 to 20 amino acids. Thus, since the full sequence of peptidic membrane binding element is not disclosed in the independent claim 9, then in the dependent claim 22, the 8 to 20 amino acids that are included in the peptidic membrane sequence are also unknown and thus the claim is overly broad. Further, there is no correlation between the structure of those fragments and their function and thus the written description requirement is not satisfied.

All dependent claims are included in this written description rejection because they depend from rejected independent claim 9 and do not cure the deficiencies of the independent claim.

Claims 9, 14, 16, 18-22, and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for peptidic membrane binding element comprising SEQ ID NOs:7-11, does not reasonably provide enablement for all other undisclosed peptide membrane-binding elements that have basic amino acids and non-peptidic membrane binding elements with acyl groups. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In *re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) eight factors should be addressed in determining enablement.

1.) The nature of the invention: the invention is a method for preparing an organ by perfusion prior to transplantation or storage of the organ where a fragment comprising any sequence of SEQ ID NO:1 is used having complement inhibitor activity, and a non-peptidic membrane binding element is used that has acyl groups, and where also a peptide membrane binding element is used that has basic amino acids in its structure.(see claim 9)

2.) The breadth of the claims: the claims are extremely broad in that a very large number of constituents could be encompassed by any structure of non-peptidic

membrane binding elements that have acyl groups or any structure of peptide membrane binding elements that have only at least 2 basic amino acids in its sequence.

3.) the predictability or unpredictability of the art: / 7.) The state of the prior art: the prior art teaches different compositions that comprise CR1 in combination with other moieties. The art is unpredictable because the variety of non-peptide membrane binding elements that have acyl groups is almost endless, and also the variety of peptide membrane binding elements that have at least 2 basic amino acids is endless.

4.) & 5.) The amount of direction or guidance presented:/The presence or absence of working examples: there is no disclosure of a correlation between function and structure of a fragment comprising any sequence of SEQ ID NO:1 having complement inhibitor activity, or non-peptidic membrane binding element and its function, or peptide membrane binding element and its function, since the structures claimed are not specific and thus do not correlate to their specific functions.

6.) The quantity of experimentation necessary: there is a large quantity of experimentation necessary to determine which structures that are claimed would have the desired function necessary for the instant invention to be successfully performed or used.

8.) Level of skill in the art: the level of skill in this art is high, at least that of a doctoral scientist with several years of experience in the art.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented.

Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9, 14, 16, 17, and 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Rittershaus et al. (U.S. 6,193,979 B1). Rittershaus et al. teach that compositions that comprise a complement-related protein (CR1) in combination with the Lewis X antigen or the sialyl Lewis X antigen, a carbohydrate moiety. See Abstract.

Rittershaus et al. teach a soluble CR1 peptide, sCR1, and their use where organs prepared for transplant are perfused with the peptides. Alternatively, organs(from a cadaver, for example) for transplantation are stored in solutions containing the peptides (see column 36, line 15). (instant claims 9, 19-22)

In column 33, lines 21-24, it is taught that carbohydrate side chains of complement glycoproteins maybe selectively oxidized to generate aldehydes. Examiner would like to point out that aldehydes contain acyl groups and thus claim 9 is anticipated because here, a non-peptidic membrane binding element comprises acyl group, for example).

Rittershaus et al. teach formulations of the peptides with excipents including, for example, pharmaceutical grades of mannitol (see column 37 regarding claim 14).

The soluble CR1 peptides of Rittershaus et al. would inherently comprise SCRs, the sequence of 2 to 197 of SEQ ID NO:1, and membrane binding elements consistent with claims 16-17. Thus, the reference clearly anticipates the invention as recited in the claims.

Further, in Figure 4, column 11, Rittershaus et al. describes the protective effects of sCR1 from lung injury induced by CVF; where Figure 4B shows the measurement of the reduction over control of hemorrhage assured by a red blood cell leakage into the lung from the blood vessel, for example. (see column 11 regarding claims 19-21).

Claims 9, 17, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. (U.S. 6,713,606 B1). Smith et al. teach CR1, which would comprise SCRs and membrane binding elements consistent with claim 17. Further, Smith et al. teach soluble CR1 polypeptide that is derivatized with a myristoyl group (See column 17, line 55 regarding claim 18). At column 18, Smith et al. teach the use of peptides for Post-Ischemic Reperfusion Conditions. Thus, the reference clearly anticipates the invention as recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 14, 16-21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Rittershaus et al. (U.S. 6,193,979 B1) in view of Smith et al. (U.S. 6,713,606 B1). Rittershaus et al. teach compositions that comprise a complement-related protein (CR1) in combination with the Lewis X antigen or the sialyl Lewis X antigen, a carbohydrate moiety. Rittershaus et al. teach a soluble CR1 peptide, sCR1, and their use where organs prepared for transplant are perfused with the peptides. Alternatively, organs for transplantation are stored in solutions containing the peptides (see column 36, line 15). Rittershaus et al. teach formulations of the peptides with excipents including, for example, pharmaceutical grades of mannitol (see column 37 regarding claim 14). The soluble CR1 peptides of Rittershaus et al. would inherently comprise SCRs, the sequence of 2 to 197 of SEQ ID NO:1, and membrane binding elements consistent with claims 16 and 17.

Further, in Figure 4, column 11, Rittershaus et al. describe the protective effects of sCR1 from lung injury induced by CVF; where Figure 4B shows the measurement of the reduction over control of hemorrhage assured by a red blood cell leakage into the lung from the blood vessel, for example. (see column 11 regarding claims 19-21).

Rittershaus et al. do not teach complement–related protein (CR1) in combination with a myristoyl group.

Smith et al. teach soluble CR1 polypeptide derivatized with a myristoyl group (see column 17, line 55 regarding claim 18).

Claim 24 is included in this rejection because a kidney perfusion solution is commonly known and used in the art and thus one of ordinary skilled in the art would be

motivated to use the known perfusion solution to a perfusion process, which is the same method.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the myristoylated CR1 polypeptide of Smith et al. for the CR1-lewis antigen composition in the method of perfusing an organ, where the organ is a lung, a heart, or a kidney, for a prevention of ischemic reperfusion injury as taught by Rittershaus et al. A person of ordinary skill in the art would have been motivated to make the above substitution because both compositions are taught as having uses in the prevention of post-ischemic reperfusion injuries. Thus, a person of ordinary skill in the art would have expected success in perfusing an organ with the myristoylated CR1 polypeptide of Smith et al. Therefore, the claimed invention is within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Applicants' Arguments and Examiner's Response

ANTICIPATION: Applicants argue that because the reference does not teach at least two membrane binding elements wherein (a) at least one membrane binding element is a non-peptidic membrane binding element comprising acyl groups, and (b) at least one membrane binding element is a peptidic membrane binding element comprising basic amino acids, wherein the peptidic membrane binding element is bound to the non-peptidic membrane binding element and the fragment of complement receptor 1. Examiner respectfully disagrees and states that acyl groups are present where carbohydrate side chains of complement glycoproteins may be selectively

oxidized to generate aldehydes and aldehydes have acyl groups in their structure. Therefore, the rejection is proper.

OBVIOUSNESS: Applicants also discuss the rejection over Smith et al. where they state that Smith et al. discloses soluble derivatives of soluble peptides that can be used according to the invention where the instant claims are not solely directed to such composition but to methods of use for the soluble derivatives. However, the rejection over Smith is correct because Smith et al. teach that: 1) CR1 and membrane binding elements are consistent with claim 17; 2) soluble CR1 polypeptide is derivatized with a myristoyl group consistent with claim 18; and 3) the claimed peptides are used for Post–Ischemic Reperfusion Conditions. Thus, the reference clearly anticipates the invention as recited in the claims.

Applicants further discuss obviousness rejection that examiner did not provide factually-supported rationale for performing a method that would require substituting Rittershaus et al. transplant compound with Smith et al. compound. However, as stated in the rejection, a person skilled in the art would have been motivated to make the above substitution because both compositions are taught as having uses in the prevention of post-ischemic reperfusion injuries, thus one would expect a great success in perfusing an organ with the myristoylated CR1 polypeptide of Smith et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished applications is available through Private PAIR or Public PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AR

KATHLEEN KERR BRAGDON, PH.D.
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